A Dissertation on

STUDY OF HYPERTENSION AMONG URBAN FEMALE PATIENTS WITH TYPE 2 DIABETES MELLITUS

submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

in partial fulfilment of the regulations

for the Award of the Degree of

M.D. (GENERAL MEDICINE)

BRANCH - I

KILPAUK MEDICAL COLLEGE

CHENNAI

MARCH - 2008

CERTIFICATE

This is to certify that the study entitled '**STUDY OF HYPERTENSION AMONG URBAN FEMALE PATIENTS WITH TYPE 2 DIABETES MELLITUS'** is a bonafide work done by **DR.S.SRIVIDHYA,** Post Graduate Student, Department of Internal Medicine, Kilpauk Medical College, Chennai – 600 010, under my direct guidance and supervision in fulfillment of the regulations of the **TAMIL NADU DR.MGR MEDICAL UNIVERSITY** for the award of MD Degree Branch I, part II (General Medicine) during the academic period from May 2005 to March 2008.

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ACKNOWLEDGEMENT

I sincerely thank **Professor Dr.M.Dhanapal., MD., DM., (Cardio) Dean, Kilpauk Medical College** for permitting me to use the resources and clinical material of this hospital.

I also thank **Professor Dr. G. Rajendran., MD., Head of the Department of Internal Medicine, Kilpauk Medical College,** for granting me permission to conduct this study and for his guidance and encouragement.

I am very thankful to **Professor Dr.N.Gunasekaran., MD., DTCD. Department of Internal Medicine, Kilpauk Medical College,**, who for being a source of inspiration and for his invaluable suggestions and corrections at every stage of this study.

I am grateful to the **Assistant Professors Dr.P.Paranthaman., MD., DTCD., Dr.G.Ranjani., MD.,** and **Dr.S.Kalaichelvi., MD., DGO., Department of Internal Medicine** for the help and advice given to me over the last three years.

I am especially thankful to **Dr.Pushpa Masiwal., D.Diab., Assistant Professor, Department of Internal Medicine** for providing useful information and insights during the study.

I also thank my fellow post graduates and house surgeons for all the help they rendered.

Last but not the least, I render my heartfelt thanks to all the patients, without whom this study would not have been possible.

CONTENTS

INTRODUCTION

Diabetes mellitus is a colossal health problem in India today, thanks to the changing lifestyle and dietary habits. Hypertension is another disease with a smouldering course, which synergises with the deleterious effects of diabetes[1]. The incidence of both these diseases has escalated among all age groups in recent years.

The association between central distribution of fat and diabetes was observed by Vague, in 1956. The discovery of the role of insulin resistance in Type – 2 DM by Reaven et al.,[2] opened up wide areas of study about the prevention of diabetes and its complications. The importance of meticulous blood pressure control in Diabetes was stressed by Carl –Erik Morgan and Hans Henrik Parving[3].

Western studies show that 30.5% of Type 2 DM patients and 20.40% of patients with Impaired Glucose Tolerance (IGT) are hypertensive. Hyperinsulinemia and insulin resistance are the main

causes for this. There is compelling evidence for marked ethnic differences in the cardiovascular morbidity in Type 2 DM patients with metabolic syndrome. South Indians are more prone to complications of Type 2 DM compared to Caucasians with similar weight range and body mass index.

Aim of study

AIM OF STUDY

1. To assess the blood pressure profile among urban female Type 2 DM patients.

2. To identify the blood pressure range in relation to age, duration and complications of Type 2 DM.

3. To find out the pattern of hypertension among Type 2 DM patients.

4. To motivate for intensive therapy and blood pressure control.

Review Of Literature

REVIEW OF LITERATURE

Definitions

Diabetes

Diabetes mellitus is a heterogeneous group of disorders characterized by chronic hyperglycemia, with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, action or both.

Criteria for the diagnosis of diabetes mellitus[4]

- Symptoms of diabetes plus random blood glucose concentration >11.1 mmol / lit (OR)
- Fasting plasma glucose $\geq$ 7.0 mmol / lit (OR)
- Two hour plasma glucose $\geq$ 11.1 mmol / lit during an oral glucose tolerance test using 75 gm glucose load.

Hypertension

Hypertension is defined as the presence of a blood pressure elevation (BP) to a level, that places patients at an increased risk of target organ damage at several vascular beds, including retina, brain, heart, kidney and large conduit arteries.

Classification of blood pressure for adults ≥18 yrs (Joint National Committee VII)[5]

Category	Systolic pressure (mmHg)	Diastolic pressure (mmHg)
Normal	< 120	< 80
Pre hypertension	120 – 139	80 - 89
Hypertension		
Stage 1	140 – 159	90 - 99
Stage 2	≥160	≥100

- Isolated systolic hypertension – systolic BP ≥ 140 and diastolic BP < 90 mmHg.

Metabolic Syndrome

It consists of insulin resistance, glucose intolerance, a characteristic dyslipidemia – hypertriglyceridemia, low High Density Liproprotein (HDL) Cholesterol and raised Low Density Lipoprotein (LDL), with an excess of small dense LDL particles, truncal obesity, procoagulant changes and hyperuricemia [2,6,7].

Adult Treatment Panel – III criteria for diagnosis of the metabolic syndrome[8]

1. Central obesity	-	Waist $\geq$ 102 cm (men)
		$\geq$ 88 cm (women)
2. Blood pressure (mmHg)		>130/85 or treated for hypertension
3. Dyslipidemia (mmol / lit)	-	Triglycerides $\geq$ 1.7
		HDL – cholesterol < 1.0 (men), < 1.3 (Women)

4. Dysglycemia (mmol / lit) - Fasting plasma glucose $\geq$ 6.1

Note : Three or more factors – diagnostic

WHO criteria for diagnosis of metabolic syndrome

Presence of diabetes and / or insulin resistance with two of the remaining factors

1. Central obesity	WHR $\geq$ 0.9 (men), 0.85 (women) and / or BMI > 30 kg/m^2
2. Blood Pressure	$\geq$ 140/90 mm Hg
3. Dyslipidemia (mmo1/lit)	Triglyceride $\geq$ 1.7, HDL < 0.9 (men), <1.0 (women)
4. Hyperglycemia (mmol/lit)	Fasting glucose $\geq$ 6.1 and / or 2 hour post challenge glucose $\geq$ 7.8
5. Insulin resistance	Glucose uptake during hyperinsulinemic euglycemic clamp, in lowest quartile of population

6. Other factors	Microalbuminuria (urine albumin excretion rates > 20 μg / min or albumin : creatinine ratio > 30 mg / gm)

Epidemiology

Of the estimated 155 million diabetics in the world, 100 million live in the Indian subcontinent and China[9]. India with an estimated 40.9 million diabetics, has earned the dubious distinction of being the Diabetic capital of the world. This number is estimated to rise to 69.9 million by the year 2025[10].

The Indian Council of Medical Research (ICMR) study on the prevalence of type 2 diabetes (1972 – 75) showed a prevalence rate of 21% in urban, and 1.5 % in rural people below the age of 40[11] and 5% in urban and 2.8% in rural areas in those above 40yrs of age. The National Urban Diabetes Survey (NUDS), conducted in six metropolitan cities across India, revealed a high prevalence rate of 13.5% in Chennai[12]. The Chennai Urban Rural Epidemiology Study (CURES) showed a 15.5% prevalence of diabetes using WHO criteria[13]. The CURES reported a temporal shift in the age at diagnosis.

Studies in female patients show that, prevalence of HT is greater among post menopausal women. A meta analysis of data from 61 prospective observational studies on mortality from vascular disease, among subjects with DM without previous vascular disease, showed that BP levels are strongly associated with age specific mortality rates from ischemic heart disease and other vascular causes. Men and women with high normal BP at the baseline examination, had a higher incidence of cardiovascular disease on follow up than those with optimal blood pressure. Complications like coronary artery disease, stroke, peripheral arterial disease, nephropathy, retinopathy, neuropathy and cardiomyopathy are more common in patients with hypertension as well.

Association between Diabetes and Hypertension

- HT in Type -2 DM
- HT associated with nephropathy and Type – 1 DM.
- Coincidental Hypertension in DM
    - Essential HT
    - Isolated systolic HT

- Renal scarring

- Diabetogenic anti – hypertensive drugs
  - Thiazide diuretics
  - Beta blockers

- Drugs causing HT and glucose intolerance
  - glucocorticoids
  - Oral contraceptive pills

- Endocrine disorders causing HT and glucose intolerance
  - Acromegaly
  - Cushing's syndrome
  - Conn's syndrome
  - Pheochromocytoma

Metabolic disorders associated with HT and DM

- Central Obesity
- Microalbuminuria
- Low HDL cholesterol
- High triglyceride levels
- Insulin resistance
- Left ventricular hypertrophy
- Increased C-Reactive Protein
- Endothelial dysfunction
- Increased apolipoprotein – B levels
- Increased fibrinogen levels
- Increased plasminogen activator inhibitor – 1 levels
- Increased uric acid levels

Peculiar characteristics of HT in type – 2 DM[14]

1. Increased salt sensitivity

Sensitivity to dietary salt in greatest, in those with diabetes, renal insufficiency, low renin status, African Americans and the elderly[15,16]. This inturn leads to volume expansion in those with unrestricted salt intake.

2. Loss of nocturnal dip in BP

Normotensives and most hypertensives have a circadian pattern of blood pressure and heart rate during 24 hour ambulatory monitoring[17]. BP is highest in awake state and lowest, (falls by 10-15%) during sleep, a pattern called 'dipping'. Diabetics have a <10% decline in BP at night[18] and this attributes to an increased risk of stroke and myocardial infarction. Therefore, drugs providing consistent and sustained 24 hour BP control will be advantageous[19].

3. Microalbuminuria

In type 2 DM, microalbuminuria is associated with insulin resistance, salt sensitivity, loss of nocturnal dipping and left ventricular hypertrophy. Increased systolic BP is an important determining factor in the progression of microalbuminuria[20].

4. Isolated systolic hypertension

As atherosclerosis progresses in type 2 DM, larger arteries lose elasticity and become rigid. The arterial system is incapable of expansion for any given volume of blood ejected from the left ventricle and the systolic BP rises disproportionately. Isolated systolic hypertension thus occurs, at a younger age in diabetics.

5. Orthostatic hypotension

In normal individuals pooling of blood in the periphery, causes fall in stroke volume and systolic BP and rise in systemic vascular resistance, diastolic BP and heart rate on standing. This phenomenon is exaggerated in diabetics, leading to orthostatic hypotension, which in turn causes cerebral hypoperfusion.

In hyperadrenergic diabetics, orthostatic hypertension occurs. β blockers are undesirable in such patients. Clonidine might blunt such a response[21].

PATHOGENESIS OF HYPERTENSION IN TYPE -2 DM

The state of hyperinsulinemia that exists in type 2 DM is associated with generation of reactive oxygen species[22] that scavenge Nitric Oxide (NO) and impair its bioactivity. This leads to defective endothelium dependent vasodilatation and plays a key role in progression of atherosclerosis[23]. Moreover, inability to counteract platelet derived growth factor activity and promotion of phenylation of RAS proteins precipitate atherosclerosis[24].

Insulin also acts on the distal renal tubule to retain Na^+ ions and water [23,25]. It also stimulates the cell membrane Na^+ - K^+ adenosine triphosphatase, which raises intracellular Na^+ in vascular smooth muscle, by increasing cytosolic Ca^{2+} levels. This directly enhances contractility and peripheral vascular resistance[26,27]. Insulin stimulates proliferation of vascular smooth muscle cells, which results in medial hypertrophy and ultimately leads to hypertension[28].

The main determinants of hypertension in a patient with Type 2 DM are total body fluid volume, sodium content, insulin levels and glucose levels.

Sodium and total body fluid volume

Total body exchangeable sodium in diabetic patients is 10% higher than non diabetics. The increase in exchangeable sodium is explained partially by active reabsorption of glucose and ketones in the kidney, as sodium salts. Increased extracellular osmolarity caused by hyperglycemia leads to water retention in the vascular space.

Diabetes is associated with decreased Plasma Renin Activity (PRA), compared to normal individuals. Impaired β - adrenergic regulation of renin secretion and decreased prostacyclin secretion contribute to low PRA in Diabetes Mellitus. Moreover, inactive renin is increased in DM and is associated with an increased incidence of microvascular disease. Hyporeninemic hypoaldosteronism seen in diabetic nephropathy is associated with elevated arterial pressure and hyperkalemia. Despite the Low PRA activity, the Renin – Angiotensin – Aldosterone system seems to contribute to the pathogenesis of hypertension. Increased activity of tissue Renin Angiotensin System,

especially vascular renin with local generation of Angiotensin II and enhanced arterial sensitivity to renin, has been proposed as possible mechanisms.

Though Atrial Natriuretic Peptide (ANP) levels are relatively high among diabetics, its action can be blunted. This could promote sodium retention and hypertension. This is another theory postulated. The increased ANP levels can promote glomerular hyperfiltration in diabetics and lead to hypertrophy in course of time.

Erythrocyte Sodium – Lithium counter transport system activity is increased in Type 2 DM. This leads to increased Sodium reabsorption in proximal convoluted tubules of the kidney.

Insulin and Diabetic hypertension

Hypertension is associated with hyperinsulinemia in obese diabetics, non diabetic obese individuals and essential hypertension. Reduced tissue response to insulin is the key factor leading to hyperinsulinemia. There is a negative correlation between insulin sensitivity and systolic blood pressure. Presence of hypertension in diabetics further aggravates insulin resistance.

Type 2 DM patients have reduced glucose uptake through the oxidative pathway and reduced effects of insulin on suppression of hepatic glucose output. Truncal adiposity without marked increase in BMI, is linked with HT and hyperinsulinemia. Intraabdominal adipocytes readily release Free Fatty Acids in response to adrenergic stimulation, due to increased sensitivity of omental adipocytes to β3 adrenergic stimulation. Increased Fatty Acids inturn impair hepatic insulin clearance, and muscle glucose uptake, and is associated with increased vascular reactivity. Increased Free Fatty Acids also increase sensitivity to α1 adrenoreceptor mediated vasoconstriction. Activation of protein kinase – C, increased generation of cyclooxygenase metabolites and inhibition of Nitric Oxide production lead to this process of vasoconstriction.

Normally, insulin stimulates muscle blood flow by its vasodilatory effect and this facilitates glucose delivery and uptake. In Type 2 DM, due to specific impairment of sympathetic neural responsiveness in skeletal muscle, insulin fails to enhance muscle blood flow. This could lead to diminished peripheral blood flow and glucose delivery and contribute to hypertension.

Increased serum leptin levels in diabetics is directly related to Blood Pressure and heart rate. Insulin increases Vascular Smooth Muscle Cell cytosolic calcium, through activation of voltage dependent calcium channels. The mitogenic effect of insulin on vascular smooth muscle cells, further enhances their proliferation. Proinsulin, the precursor of insulin stimulates endothelin secretion and also increases tissue Plasminogen Activator Inhibitor (PAI) in endothelial cells. These mechanisms lead to early development of hypertension and also enhance coagulation.

Insulin increases LDL binding to smooth muscle cells, fibroblasts and monocytes. Monocytes, are the precursors of foam cells. In these cells, insulin stimulates the activity of 3-hydroxy – 3 methyl glutaryl coenzyme A (HMG – CoA) reductase, the rate limiting enzyme of cholesterol synthesis, and thus enhances atherosclerosis.

Magnesium may also mediate a nexus between HT, DM and insulin resistance. Total red blood cell magnesium levels usually increase in response to increased insulin levels. This effect is impaired in Type 2

DM. The resultant magnesium depletion downregulates the activity of rate limiting glycolytic enzymes and reduces insulin sensitivity. Reduced magnesium levels also increase vascular reactivity.

Role of Glucose in Diabetic hypertension

Increased glucose level causes upregulation of Platelet Derived Growth Factor (PDGF) receptor expression and thus exerts a mitogenic effect on vascular smooth muscle cell. It also directly enhances endothelin secretion. Glucose also exerts a direct toxic effect on endothelial cells, resulting in accelerated cell death. Angiotensin Converting Enzyme (ACE) activity is increased by glucose. Glucose mediates decrease in hydrogen peroxide scavenging and thus result in increased oxidative tress in vascular tissue. This leads to early oxidative modification of proteins in the endothelium, with loss of functions of key enzymes like glucose–6–phosphate dehydrogenase and glyceraldehyde-3-phosphate dehydrogenase. This loss of functional endothelial cells, coupled with reduced NO levels causes arterial vasoconstriction. Finally, glucose enhances LDL oxidation, which leads to increased microvascular complications.

Circulating glucose binds non enzymatically to proteins, leading to formation of highly reactive Advanced Glycosylation End Products. These in turn bind selectively with basement membrane proteins and promote vasculopathy. Advanced glycosylation end products also promote the progression of medial hypertrophy and inhibit the vasodialatory effect of NO.

Impact of Hypertension in Diabetes

Many hypertensive diabetic patients show signs of target organ damage mainly affecting the cardiovascular system[29]. Deaths from coronary heart disease increase by 2-5 times in diabetics with hypertension. Impaired left ventricular relaxation and increased left ventricular mass[30] are independent predictors of death from coronary heart disease.

Hypertension also predisposes to nephropathy and retinopathy. Diabetics should therefore be screened on diagnosis and atleast annually there after, for hypertension.

TARGET BLOOD PRESSURE IN TYPE 2 DM

The Hypertension Optimal Treatment (HOT) trial and UKPDS demonstrated that, patients assigned to lower BP levels, had improved outcome, particularly, in stroke prevention [31]. A target BP of <130/80 is recommended by the Seventh Joint National Committee (JNC) on prevention, detection, evaluation and treatment of high BP and by the American Diabetic Association. In patients with microalbuminuria and renal insufficiency blood pressure goal is < 125/75 mm Hg.

INVESTIGATION OF HYPERTENSION IN TYPE 2 DM

i. Rule out rare causes of secondary hypertension

ii. Cardiac function assessment

- 12 lead Electrocardiogram
- Echocardiography
- Exercise testing / Stress echo cardiogram
- 24 hour holter monitoring

iii. Renal function assessment

- Microalbuminuria
- look for cellular casts in urine
- Blood urea nitrogen and serum creatinine estimation
- Glomerular Filtration Rate Measurement
- Isotope renogram to look for renal artery stenosis (or) Renal doppler studies

iv. Lipid profile

MANAGEMENT OF HYPERTENSION IN TYPE 2 DM

Non pharmacological therapy

- Exercise – aerobic physical activity
- Smoking cessation
- Adequate Potassium and Magnesium intake
- Alcohol intake <1 ounce / day

- Diet rich in fruits and vegetables and low in fat

- Reduced sodium intake < 100 mmol / day.

Pharmalogical treatment

Diuretics

Furosemide, bendroflumethiazide, spironolactone and indapamide are suitable for use in diabetics. Lower dosages should be used, in combination with potassium supplements or potassium sparing drugs. Thiazides may aggravate dyslipidemia and hyperglycemia and should be used with caution[32].

Beta blockers

Beta blockers lower BP, heart rate and cardiac output. But, they may aggravate hyperglycemia and dyslipidemia through inhibition of β-2 adrenergic mediated insulin release and decreased insulin action in peripheral tissues. They may also interfere with the counterregulatory effects of catecholamines, causing hypoglycemia unawareness.

Recent studies show that metoprolol and carvedilol[33,34] can be used favourably in cardiac failure patients[35]. In the UKPDS, atenolol was comparable to captopril[36].

Calcium channel antagonists

Nondihydropyridine calcium channel antagonists reduce proteinuria in diabetic nephropathy. They are also indicated in patients with angina or supraventricular tachycardia. They are better at preventing stroke than beta blockers and thiazide diuretics[37].

Angiotensin – Converting Enzyme (ACE) inhibitors

ACE inhibitors may improve insulin sensitivity [38]. Hypoglycemia is rarely reported[39].

They reduce albuminuria and delay progression of renal damage in nephropathy[40]. They improve left ventricular function. Ramipril reduces cardiovascular morbidity in diabetics, with or without preexisting heart disease[41]. However, they may precipitate Acute Renal Failure in elderly and cause potassium retention. So creatinine and K^+ levels should be monitored periodically.

Angiotensin Receptor Blockers (ARB)

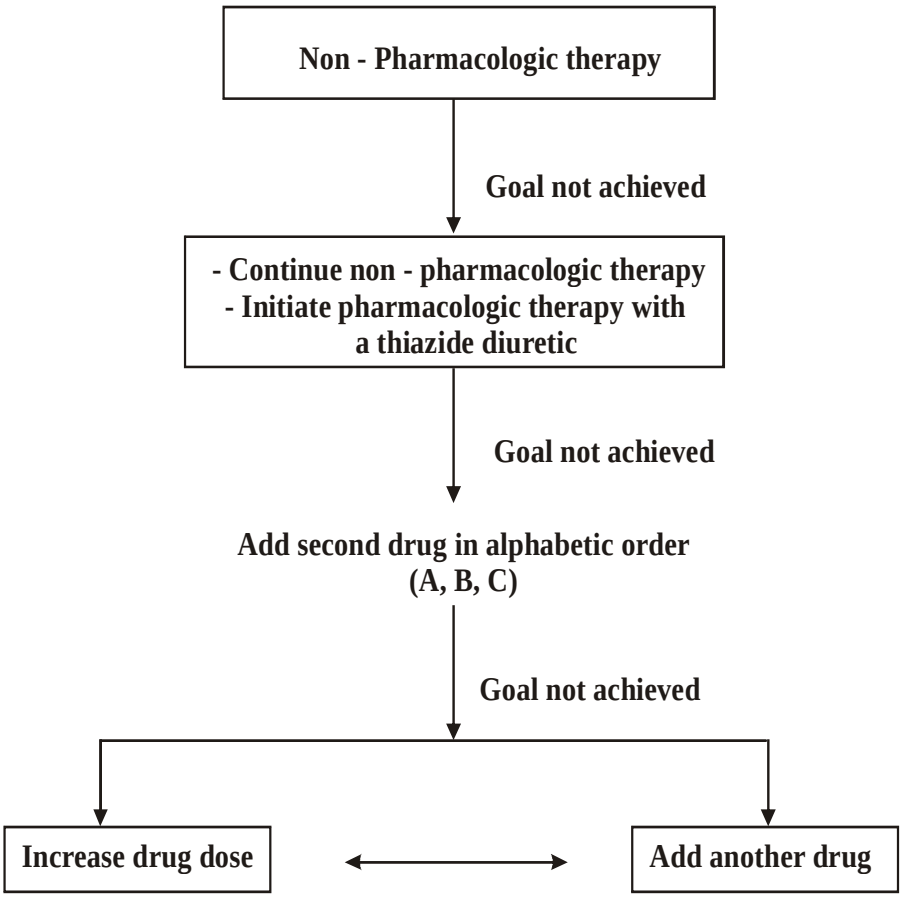
They slow the progression of nephropathy in diabetes patients with albumunuria[42]. Losartan is better than atenolol in reducing total mortality in type 2 DM patients with HT and left ventricular hypertrophy[43].

Alpha -1 Adrenoreceptor antagonists

They can improve dyslipidemia and insulin senstitivity and lower BP effectively.

TREATMENT ALGORITHM FOR HT IN TYPE 2 DM

Treatment goal – BP < 130/80



A - ACE inhibitor / Angiotensin Receptor Blocker

B - Beta Blocker

C - Calcium channel blocker

Identification of the antihypertensive agent of choice for Type 2DM may appear rather questionable since multiple drugs are required in most patients to achieve the target of < 130/80, as observed by Kaplan. In the HOT study, the large majority of patients randomized to a diastolic BP < 80 mm Hg were on double or triple drug therapy. Likewise, in the UKPDS, 29% of the patients randomized to tighter BP control, were on three drugs and 34% were on two drugs. Studies on diabetic nephropathy, revealed that most patients were on 2 to 3 drugs in addition to an Angiotensin Receptor Blocker.

OUTCOME OF TREATING HYPERTENSION IN DM

Effective treatment of hypertension slows down the progression of diabetic nephropathy, by lowering albumin excretion and the rate of fall of glomerular function. As per the UKPDS study, tighter BP control causes significant reduction in the risk of stroke (44%) heart failure (56%), myocardial infarction and peripheral vascular disease. Interestingly the most powerful effects were related to reduction in the two major microvascular complications – nephropathy and retinopathy. Thus effective treatment seems to be cost effective as per the health conomics analysis in UKPDS[45].

The Bergamo Nephrologic Diabetes Complications Trial, concluded that in subjects with Type 2 DM with hypertension, normoalbuminuria and normal renal function, ACE inhibitor therapy with trandolapril and verapamil (or) trandolapril alone, prevented the onset of microalbuminuria. The Reduction of Endpoints in NIDDM with the Angiotension II Antagonist Losartan (RENAAL) study showed that Losartan therapy was associated with a 28% reduction in the risk of End Stage Renal Disease and a 25% reduction in doubling of serum creatinine level in patients with early diabetic nephropathy.

Materials and Methods

MATERIALS AND METHODS

Setting

The study was conducted, among outpatients attending the Diabetology department in Govt. Royapettah Hospital.

Study Population

The study was conducted over an eight month period from December 2006 to July 2007. 80 female patients were selected randomly. Cases of Impaired Glucose Tolerance and Impaired Fasting Glucose were excluded. Patients with Type 2 DM for atleast one year were chosen. Informed consent was obtained from all patients.

Those with BP $\geq$ 140/90 on the first visit were reviewed twice and those with persistently high values were diagnosed as hypertensive. Patients with history of hypertension who were already on treatment, were also included among hypertensives. Of the 85 patients, chosen, three were found to be hypothyroid, one had congenital heart disease and another had chronic kidney disease and were excluded.

Inclusion criteria

Patients with Type 2DM for atleast 1 year who were on regular treatment with oral hypoglycemic agents or insulin or both.

Exclusion criteria

- Patients of age < 30
- Patients with congenital heart disease
- Pregnant women
- Cases of hypothyroidism
- Smokers

Basic data including name, sex, occupation, income, present and past history was obtained. Anthropometric measurements including height in metres, weight in kilograms, waist and hip circumference in centimeters was noted. Waist circumference was recorded, as the smallest circumference between the lower costal margin and iliac crest. Hip circumference was recorded at the widest part of the gluteal region. Vital signs were recorded. BP recordings were repeated on 3 different

occasions in patients with BP $\geq$ 140/90 on the first visit. Only those with persistently elevated values and those with a history of Hypertension were included among hypertensive. General and detailed systemic examination was done in all patients. Renal parameters, urine examination, electro cardiogram and chest X-ray was done in all patients.

Reference values used

- Hypertension - BP $\geq$ 140/90 mm Hg (or) H/o hypertension on treatment

- Total cholesterol < 200 mg/dl - Normal

- BMI

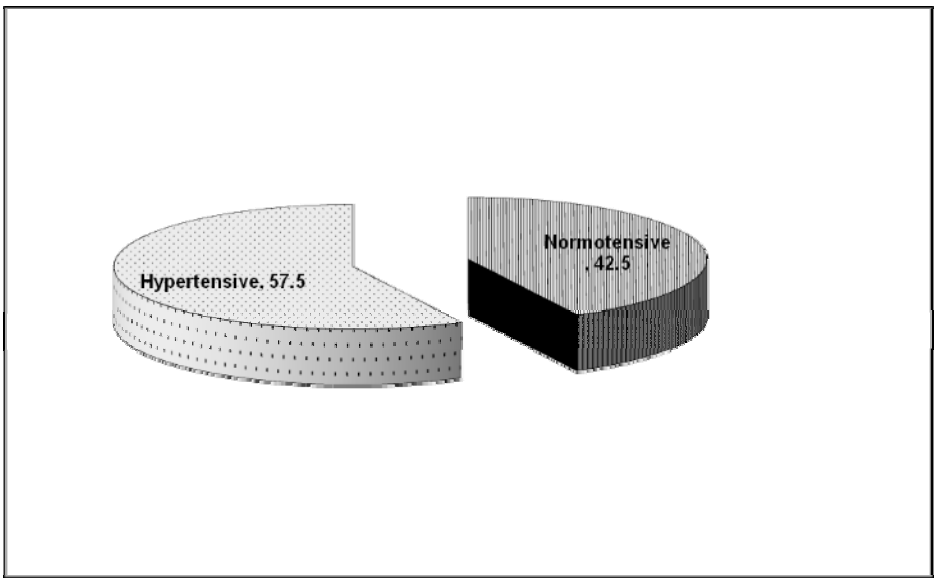
  Values $\geq$ 25 kg / m^2 i.e. overweight and obese taken as abnormal.

- WHR > 0.85 was taken as indicator of abdominal obesity.

Observation and Analysis

OBSERVATIONS AND ANALYSIS

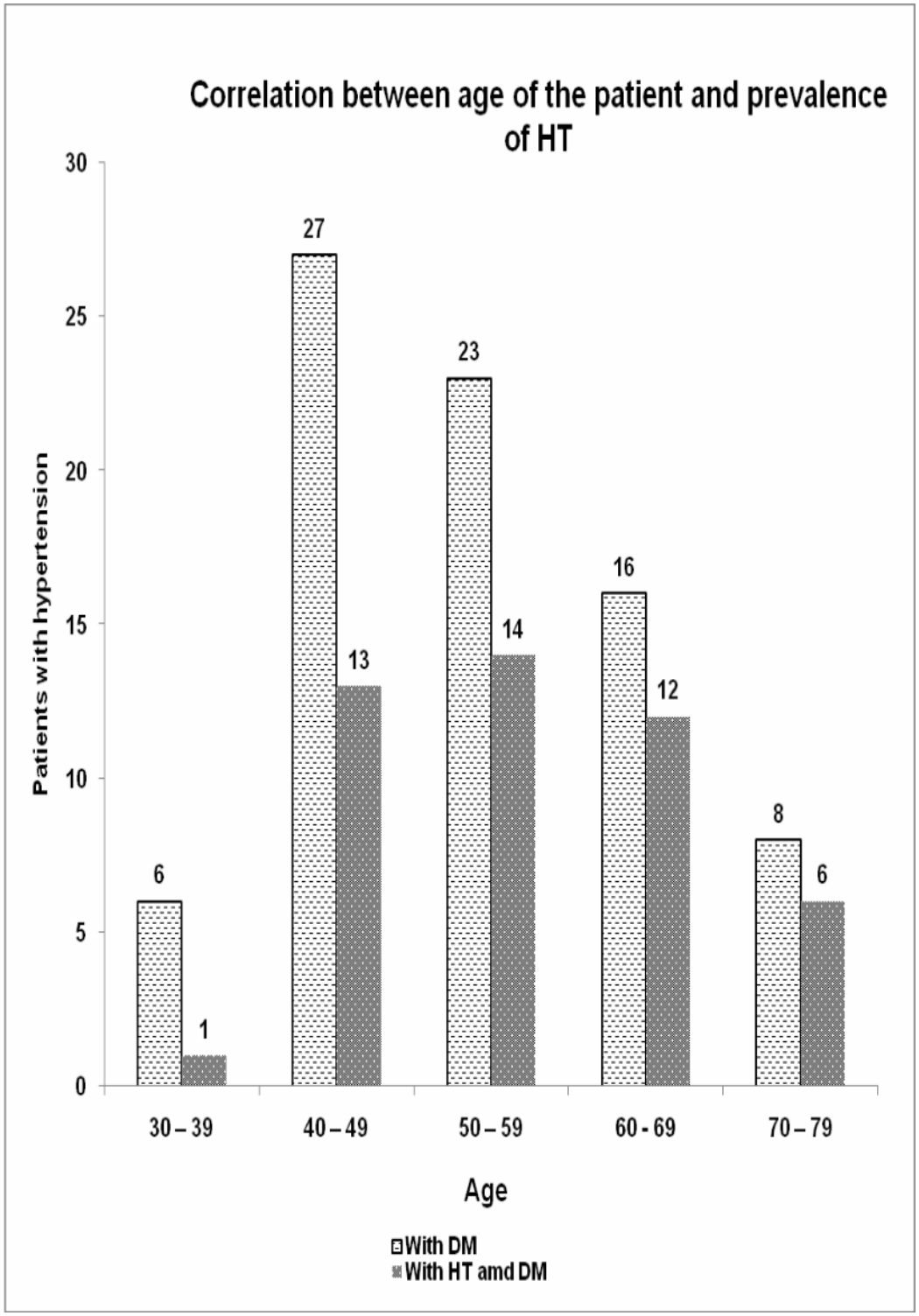
Among the 80 patients included in the study 57.5% (46 subjects) were hypertensive. Another 15% (12 subjects), were noted to have BP above the ADA target range of < 130/80. Among the hypertensives approximately 45.6% were newly diagnosed.



Correlation between age of the patient and prevalence of HT

Age Group	No.of patients	No with HT	% with hypertension
30 – 39	6	1	16.7%
40 – 49	27	13	48.2%
50 – 59	23	14	60.9%
60 - 69	16	12	75%
70 – 79	8	6	75%

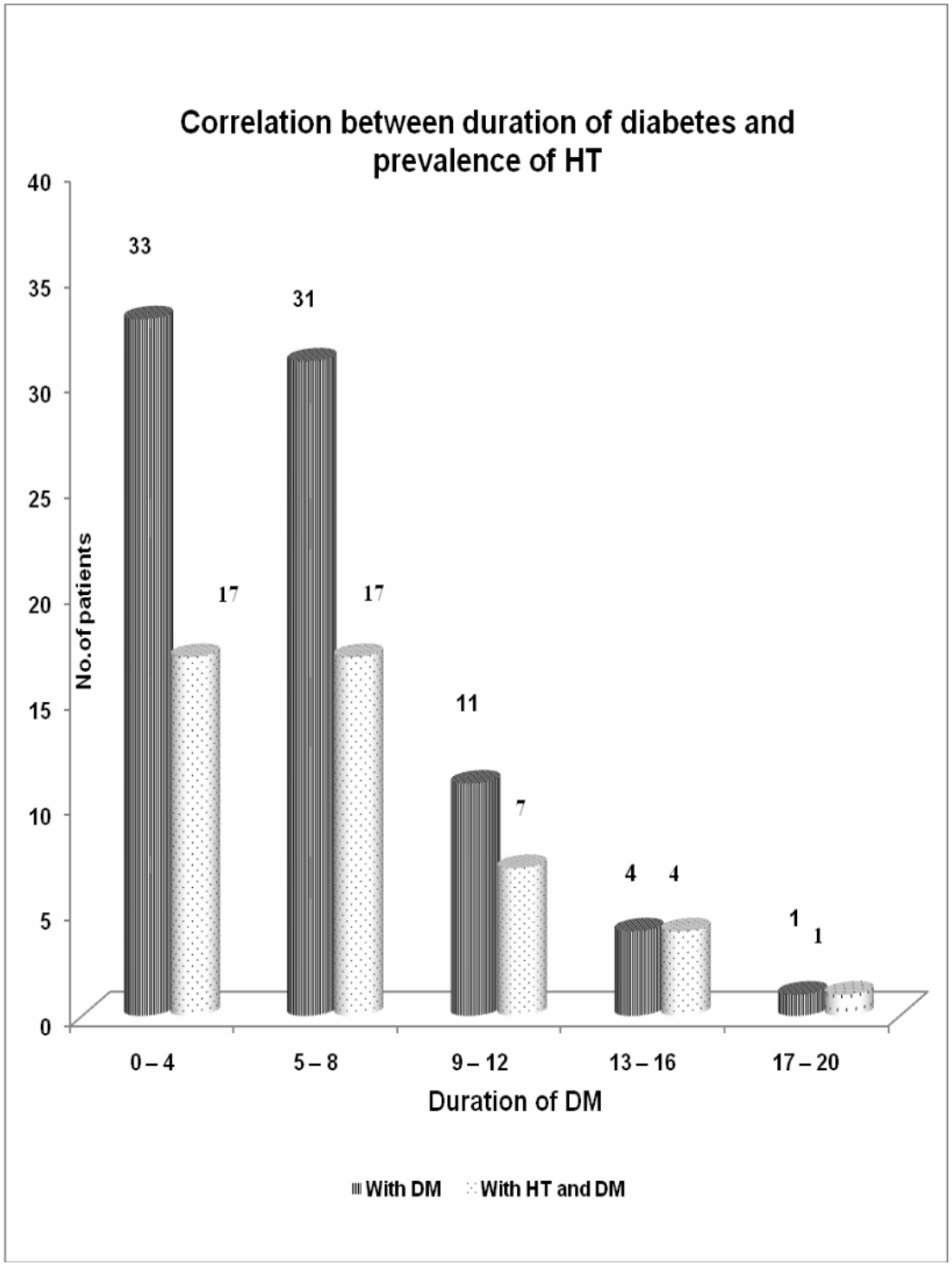
The prevalence of HT in the 30 to 39 age group was 16.7%. There was a gradual increase in prevalence of HT with increase in age. The 70-79 age group showed a prevalence of 75%


Correlation between age of the patient and prevalence of HT
Patients with hypertension
30
25
20
15
10
5
0
6
1
27
13
23
14
16
12
8
6
30 – 39
40 – 49
50 – 59
60 - 69
70 – 79
Age
With DM
With HT amd DM

Correlation between duration of diabetes and prevalence of HT

Duration of diabetes	No of patients	No with HT	% with hypertension
0 – 4	33	17	51.5%
5 – 8	31	17	54.8%
9 – 12	11	7	63.6%
13 – 16	4	4	100%
17 – 20	1	1	100%

Among the 33 patients diagnosed to have diabetes within 4 years, 51.5% were hypertensive. The prevalence was found to be as high as 100% in those with diabetes for longer duration.


Correlation between duration of diabetes and prevalence of HT
No.of patients
40
35
30
25
20
15
10
5
0
33
17
31
17
11
7
4
4
1
1
0 – 4
5 – 8
9 – 12
13 – 16
17 – 20
Duration of DM
With DM
With HT and DM

Correlation between HT and Coronary Artery Disease (CAD) in Type 2 DM

Age Group	HT	CAD	CAD+HT	% of CAD with HT
30 – 39	1	0	0	-
40 – 49	13	2	1	50%
50 – 59	14	4	2	50%
60 – 69	12	3	2	66.6%
70 – 79	6	2	2	100%
		12	**9**	**75%**

Totally 12 patients had CAD including those with ECG changes and those with symptoms of CAD. Among them 75% (9) were hypertensive.

Correlation of hypercholesterolemia with HT

Age Group	HT	↑ Cholesterol	HT + ↑ Cholesterol	% of ↑ Cholesterol with HT
30 – 39	1	1	0	-
40 – 49	13	5	2	40%
50 – 59	14	5	3	60%
60 – 69	12	2	1	50%
70 – 79	6	2	2	100%
		15	8	53.3%

Among the 80 patients, 18.7% had hypercholesterolemia. Of the 15 patients with hypercholesterolemia 58.3% (8 patients) were hypertensive.

Correlation of Cerebrovascular Accidents (CVA) and

Peripheral vascular disease (PVD) with HT

Age Group	HT	PVD	PVD+ HT	%	CVA	CVA + HT	% of CVA with HT
30 – 39	1	0	0	0	-	-	-
40 – 49	13	1	0	0	-	-	-
50 – 59	14	2	1	50%	1	-	-
60 – 69	12	1	1	100%	-	-	-
70 – 79	6	1	1	100%	1	1	100%
		5	3	60%	2	1	50%

Only 5 patients had peripheral vascular disease. Of them 60% were hypertensive. Only 2 patients in the study had history of CVA. Among them one patient was hypertensive.

In the Edinberg Artery study, systolic BP was related independently to claudication with an odds ratio of 1.2. Systolic BP was documented as a risk factor in the Framingham study as well.

Correlation of Diabetic Nephropathy, Retinopathy and Neuropathy with HT

Age Group	HT	Nephro pathy	Nephro + HT	%	DR	HT+ DR	%	Neuro pathy	Neuro + HT	%
30 – 39	1	-	-	-	-	-	-			-
40 – 49	13	1	1	100%	1	1	100%	1	-	0
50 – 59	14	2	2	100%	1	1	100%	1	1	100%
60 – 69	12	1	1	100%	2	1	50%	2	1	50%
70 – 79	6	1	1	100%	1	1	100%	2	1	50%
		5	5	100%	5	4	80%	6	3	50%

All the 5 patients who had diabetic nephropathy were hypertensive and so were 80% of those with diabetic retinopathy. Of the 6 patients with diabetic neuropathy, only 3 were hypertensive. The association with hypertension was maximum in patients with nephropathy. The prevalence of neuropathy was more common in normotensives than hypertensives.

Correlation of BMI and WHR with hypertension in type 2 DM patients

Age Group	HT	BMI ≥ 25	↑BMI + HT	%	↑ W/H Ratio	↑W/H + HT	%
30 – 39	1	3	-	-	5	1	20%
40 – 49	13	13	10	76.9%	16	10	62.5%
50 – 59	14	15	10	66.7%	17	11	64.7%
60 – 69	12	9	5	55.5%	11	10	90.9%
70 – 79	6	2	1	50%	6	3	50%
	46	42	26	61.9%	55	35	63.6%

More than 50% of the patients were overweight of whom 61.9% had hypertension. 50 patients were found to have WHR ≥ 0.85. Among them 63.6% were hypertensive. Only 42 patients were overweight, but 55 patients were found to have increased Waist Hip Ratio.

Pattern of HT among newly detected patients

Stage	No.of patients
ISH	4
I	4
II	5

ISH – Isolated systolic HT

20 patients were newly diagnosed to have HT during the study. Majority of them had stage I hypertension. 4 of them, all aged 60 and above, had Isolated Systolic Hypertension.

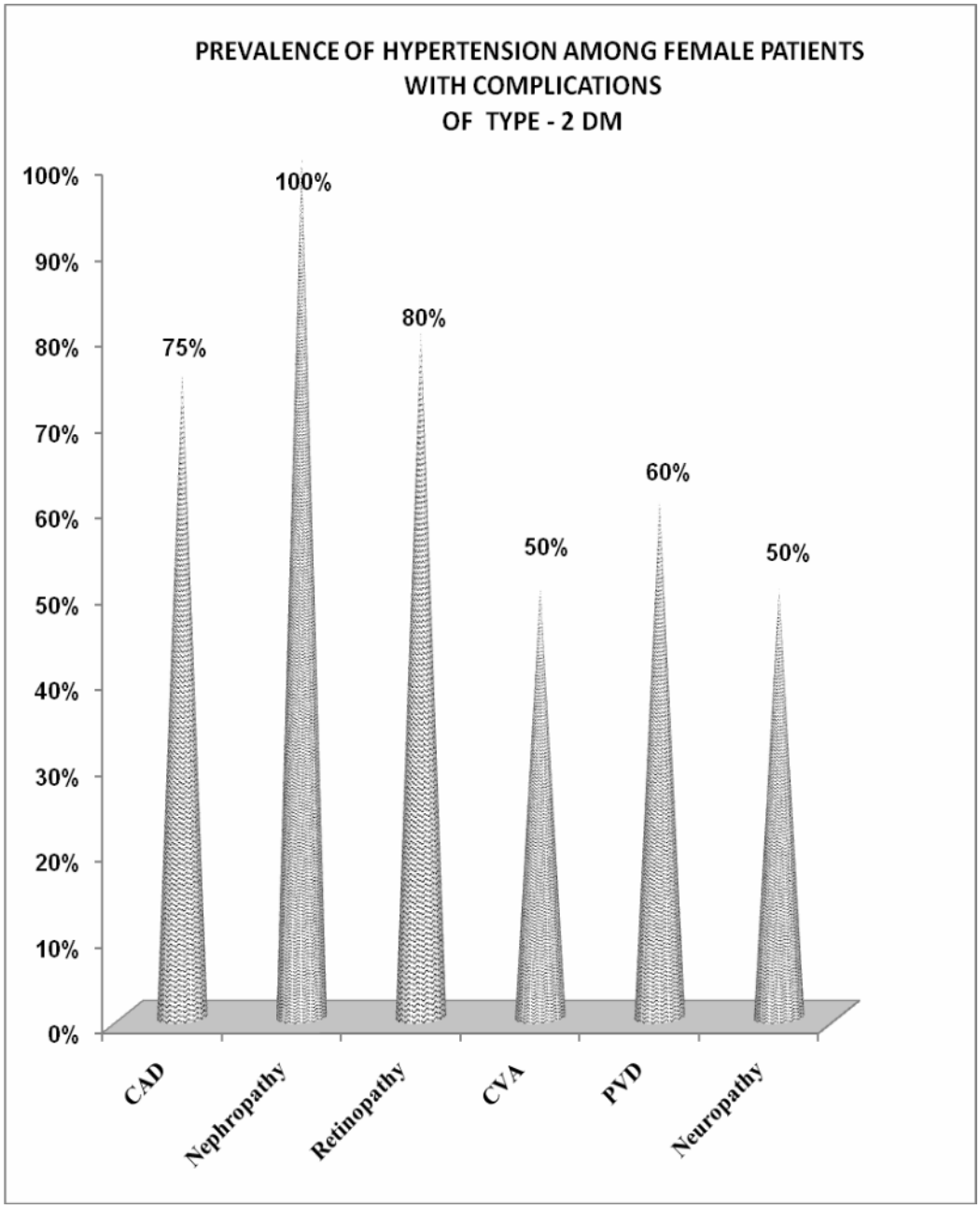
Correlation between menopausal status and hypertension

71.2% of the patients were post menopausal. Among them 65.4% were hypertensive. Only 43.5% of premenopausal females had hypertension.

Prevalence of HT among female Type 2DM patients with complications

CAD	75%
Nephropathy	100%
Retinopathy	80%
CVA	50%
PVD	60%
Neuropathy	50%

Among female patients with complications Type 2 DM, Nephropathy had maximum association with Hypertension. 80% of patients with Retinopathy and 75% of those with CAD had Hypertension. The association was less among patients with CVA and Neuropathy.


PREVALENCE OF HYPERTENSION AMONG FEMALE PATIENTS
WITH COMPLICATIONS
OF TYPE - 2 DM
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
75%
100%
80%
50%
60%
50%
CAD
Nephropathy
Retinopathy
CVA
PVD
Neuropathy

Discussion

DISCUSSION

In this study 57.5% of urban female patients with Type 2DM, were found to be hypertensive. According to WHO studies, 30.50% of those with type 2 DM have HT. The increase in prevalence in this study can be attributed to genetic and ethnic differences. Genetic susceptibility, increased prevalence of central obesity and elevated pro inflammatory markers like C-Reactive Protein (CRP) may be important causes. Moreover, levels of physical activity and fitness among South Asian females are lower, compared to Europeans.[46] Ward et al, postulated that increased glucocorticoid action in Indians with increased BMI, may be the cause for increased prevalence of HT.[47]

In this study, there was a gradual and steady increase in prevalence of HT from 16.7% in the 30-39 age group to 75% in the 70-79 age group. This is similar to the observations made by Baris et al, of the Hypertension and Diabetes Executive Committee Working Group, in which there was an increased likelihood of DM with increasing age.[48]

Vasan et al who investigated 6859 patients of the Framingham Heart Study, found that the prevalence of HT increased with duration of DM. He also observed that, even patients with a high normal base line BP, had an increase in incidence of CAD, on follow up.[49] Likewise, in this study the prevalence of HT increased from 51.5% in recently detected to 100% in those with a longer duration of DM. More over, 15 patients had BP values in the high normal range and as per the Framingham Heart study, have an increased risk of CAD.

The prevalence of CAD was observed to be 8.8% in normotensives and 19.5% in hypertensives. This was in accordance with observations by Grundy et al. He observed that risk of CAD was almost twice in patients with co-existent HT.

The total cholesterol values were elevated in only 18.75% of the diabetics in our study. Many earlier studies, revealed a normal or high normal level of total cholesterol, with increased Triglyceride and decreased HDL - cholesterol in diabetics. Due to limitation in investigation, TGL and HDL-C levels could not be assessed.

The prevalence of CVA was decreased marginally, in hypertensives (2.16%) when compared to nonmotensives (2.94%). This might be attributed to the smaller number of patients included in the study. There was a minimal increase in prevalence of peripheral arterial disease, 6.52% in hypertensive as compared to 5.55% in those who were normotensive. This was in contrast, with other studies, that show a 50% increased prevalence. Similarly, in contrast to other studies, no association was noted between HT and diabetic neuropathy, in this study.

All the patients with DM nephropathy were found to be hypertensive Retinopathy was four times more common in hypertensives compared to others.. This was in accordance with the observations made in UKPDS, where in there was a predisposition to the development of retinopathy and nephropathy in hypertensives.

More than 50% of patients in the study group were overweight (BMI $\geq$ 25). 56.5% of hypertensives were obese, as opposed to, 47% prevalence in normotensives. WHR $\geq$ 0.85 was seen in 68.8% of the study group. Among them, 63.6% were hypertensive. Similar observations were made by Bakris et al and Sower JR in their studies.

Only few studies have been conducted regarding the prevalence of DM and its complications in females. In 1984, Hartz et al., in a survey of 30,000 women reported a higher incidence of DM in women with a greater proportion of body fat in the waist. Studies by Mohan et al., show a higher body fat in Indian females compared to males.

Sex	BMI (median)	Fat % (Median)
Male	22.0	22.7%
Female	22.7	37.4%

The modified ATP III criteria for Indians suggests a waist circumferences of $\geq$ 85 cm and BP $\geq$ 130/85 for the diagnosis of metabolic syndrome in females.

Conclusion

CONCLUSION

The prevalence of HT in urban, female, South Indian population, with Type 2DM, was 57.5%.

- There was an increase in prevalence of HT with increasing age.
- Duration of DM was positively associated with prevalence of HT.
- The prevalence of obesity, particularly central obesity was greater among hypertensives.
- The prevalence of CAD in hypertensives was twice that of normotensives.
- Retinopathy and Nephropathy showed maximum association with HT.

- A considerable percentage of hypertensives (37.5%) were newly detected. Periodic screening of DM patients for HT is therefore mandatory.

- Patient with high normal BP levels who are also at increased risk of CAD must be identified and treated as per guidelines.

Summary

SUMMARY

80 urban female patients with Type 2 DM, with atleast one year duration of DM, were chosen. BP was recorded as per guidelines, and hypertensive patients were identified. BMI and WHR were calculated and patients were evaluated for complications of DM. The prevalence of complications of DM in patients with HT was compared with those with normal BP.

The prevalence of HT in urban females with Type 2DM was 57.5%. There was an increased prevalence of CAD and even greater prevalence of Nephropathy and Retinopathy in hypertensive patients. The prevalence of hypertension is more in older patients. 37.5% of hypertensives were newly detected and referred for registration in hypertension outpatient department.

Appendix

PROFORMA

Basic Data

Name : Income :

Age : Diet :

Occupation :

Anthropometry

Height : Weight : BMI :

Waist circumference :

Hip circumference : WHR:

History :

H/o DM

Duration

Treatment Details

H/o HT

H/o CAD

H/o dyslipidemia

H/o smoking and alcohol

H/o Thyroid dysfunction

H/o TIA/CVA

H/o drug intake

Family History

Obesity	Hypercholesterolemia
DM	CAD
SHT	Malignancies

Menstrual history

General Examination

Anemia

Acanthosis Nigricans

Pedal edema

Goitre

Facial puffiness

Foot ulcers

Discolouration of feet

Vital Signs

PR - Peripheral pulses -

BP - Postural fall in BP-

JVP - Resp. rate -

Systemic Examination

CVS S_1S_2 - Murmurs -

S_3/S_4 - Pericardialfriction rub -

RS

Breath sounds

Pleural rub

Added sounds

Abdomen

CNS

Fundii

Investigations

Urine - albumin

sugar

deposits

Blood urea

Serum creatinine

Blood sugar

Serum Cholesterol

Electrocardiogram

Chest X-ray

MASTER CHART

Sl. No.	Age	Age at diagnosis	Duration of DM	Ht	Wt	BMI	Waist	Hip	WHR	BP	H/oHT	CAD	Increased cholesterol	Nephro	DR	Neuro	CVA	PVD
1.	31	23	8	145	52	24.7	80	90	0.89	140/80								
2.	32	30	2	140	60	30	102	95	1.07	120/80			+					
3.	35	33	2	150	51	22.7	75	85	0.88	120/80								
4.	36	35	1	150	54	24	76	90	0.84	110/80								
5.	39	32	7	151	65	28.5	93	95	0.97	130/80								
6.	39	35	4	150	72	29.6	98	99	0.99	130/82								
7.	40	39	1	145	70	33	92	90	1.02	140/92	+	+	+					
8.	40	35	5	150	54	24	80	88	0.9	110/80								
9.	40	39	1	168	76	26.9	73	87	0.83	140/100	+							
10.	40	30	10	162	50	19	68	80	0.85	150/102	+			+	+			
11.	41	39	2	145	60	28.5	15	85	0.88	150/102	+							
12.	42	37	5	156	45	18.5	65	82	0.79	110/80			+					
13.	42	33	9	162	65	24.8	68	88	0.77	120.80								
14.	44	39	5	153	51	21.8	76	88	0.86	120/74								+
15.	44	42	1	152	57	24.6	72	83	0.86	130/86								
16.	44	35	9	150	40	17.8	63	79	0.79	136/74						+		
17.	44	39	5	156	50	20.5	71	82	0.87	110/76								
18.	45	40	5	153	56	23.9	75	88	0.85	140/92								
19.	45	42	3	157	64	26.0	78	85	0.92	170/110	+		+					
20.	45	43	2	160	63	24.6	72	82	0.87	130/80								

Sl. No.	Age	Age at diagnosis	Duration of DM	Ht	Wt	BMI	Waist	Hip	WHR	BP	H/oHT	CAD	Increased cholesterol	Nephro	DR	Neuro	CVA	PVD
21.	45	42	3	161	63	24.3	74	88	0.84	130/84								
22.	45	44	1	144	56	27.0	82	85	0.96	170/112	+							
23.	45	40	5	165	51	18.8	65	80	0.81	140/86								
24.	45	37	8	148	70	31.9	78	84	0.92	150/96	+							
25.	46	41	5	160	44	17.2	62	78	0.82	150/80								
26.	47	43	4	150	62	27.5	70	85	0.82	130/84								
27.	47	39	8	138	40	21.1	62	76	0.82	110/80			+					
28.	47	41	6	139	54	28	78	86	0.91	110/80	+							
29.	48	40	8	143	61	29.9	82	92	0.89	110/70		+						
30.	48	39	9	150	38	16.9	60	80	0.75	110/70			+					
31.	49	40	9	162	78	29.8	76	87	0.87	130/92	+							
32.	49	42	9	147	49	22.7	69	84	0.82	160/96	+							
33.	49	45	4	162	78	29.8	88	87	1.01	130/96								
34.	50	49	1	151	62	27.2	75	82	0.91	140/92								
35.	50	44	6	154	46	19.4	67	84	0.79	120/80	+							
36.	50	49	1	136	55	29.9	82	85	0.96	160/100								
37.	50	42	8	156	60	24.7	72	88	0.81	180/110	+	+					+	
38.	50	46	4	154	70	29.5	78	85	0.91	120/80	+							
39.	50	49	1	153	62	26.5	72	82	0.88	130/82			+					
40.	51	49	2	159	70	27.7	80	88	0.91	136/80	+							

Sl. No.	Age	Age at diagnosis	Duration of DM	Ht	Wt	BMI	Waist	Hip	WHR	BP	H/oHT	CAD	Increased cholesterol	Nephro	DR	Neuro	CVA	PVD
41.	52	47	5	154	70	29.5	82	85	0.96	150/110	+		+					
42.	53	51	2	154	55	23.3	66	84	0.78	150/96								
43.	53	43	10	152	56	24.2	70	84	0.83	130/84								
44.	55	45	10	154	65	27.4	84	89	0.94	150/98			+				+	
45.	55	52	3	138	41	21.6	63	80	0.79	120/80								
46.	55	48	7	153	65	27.8	76	85	0.89	110/80								
47.	55	45	10	152	60	25.9	84	89	0.94	120/80			+					+
48.	55	52	3	152	60	25.9	76	88	0.86	160/96								
49.	55	48	7	160	62	24.3	78	84	0.9	134/84								
50.	56	50	6	145	64	30.5	95	94	1.01	160/100	+							
51.	56	53	3	138	55	28.9	90	90	1.0	128/70		+						
52.	57	42	15	145	45	21.4	69	82	0.84	160/98				+	+			
53.	58	54	4	152	60	25.9	76	85	0.89	110/80								
54.	58	45	13	162	57	21.8	78	88	0.87	150/94						+		
55.	58	52	6	146	72	33.8	94	92	1.02	164/100	+	+	+					
56.	59	54	5	146	70	32.9	92	95	0.96	110/80		+						
57.	60	55	5	150	67	29.8	89	95	0.94	160/104	+		+					
58.	60	50	10	149	56	25.2	72	85	0.84	110/80						+		
59.	60	49	11	155	58	24.2	74	80	0.86	120/80	+							
60.	60	55	5	154	70	29.5	85	90	0.94	120/80								

Sl. No.	Age	Age at diagnosis	Duration of DM	Ht	Wt	BMI	Waist	Hip	WHR	BP	H/oHT	CAD	Increased cholesterol	Nephro	DR	Neuro	CVA	PVD
61.	60	57	3	150	60	24.7	73	86	0.85	132/80		+	+					
62.	60	54	6	144	58	28.0	78	86	0.90	170/88								
63.	60	55	5	154	65	31.4	84	86	0.98	120/80								
64.	60	58	2	149	55	24.8	73	80	0.91	140/94								
65.	61	46	15	152	68	29.4	78	90	0.87	140/80								
66.	62	57	5	149	55	24.8	74	84	0.88	130/90	+	+						
67.	63	60	3	164	74	27.5	75	91	0.82	130/94	+							
68.	65	51	14	152	75	32.5	90	88	0.75	150/94				+	+	+		
69.	65	62	3	152	57	24.7	87	90	0.97	146/90	+							
70.	65	60	5	154	58	24.5	70	80	0.81	140/100	+	+		+				
71.	65	63	2	144	52	25.1	68	83	0.82	140/80								
72.	65	60	5	168	76	26.6	78	84	0.92	140/96								
73.	70	69	1	151	53	23.2	66	84	0.79	140/100	+		+					
74.	71	63	8	154	64	27.0	80	92	0.87	130/80						+		
75.	74	71	3	164	60	22.3	69	84	0.82	160/98		+					+	
76.	75	70	5	152	52	22.5	76	89	0.85	110/80								
77.	76	58	18	152	79	34.2	93	93	1.0	170/120	+	+	+		+			
78.	76	66	10	148	50	22.8	72	83	0.86	160/98						+		
79.	79	73	6	156	54	22.2	76	84	0.90	144/80								
80.	79	74	5	152	65	28.1	72	84	0.85	144/90								

BIBLIOGRAPHY

1. John C. Pickup and Garreth Williams – Text book of Diabetes – 3rd edition – pg 55.2

2. Reaven GM. Role of insulin resistance in human disease. Diabetes 1988. 37 : 1595 – 607.

3. Mogensen CE. Long term anti hypertensive treatment inhibiting progression of diabetic nephropathy. BMJ 1982; 285 685-8.

4. American Diabetes Association Guidelines, 2004

5. Seventh Report of the Joint National Committee on Detection, Evaluation and Treatment, of High Blood Pressure. JAMA 289 : 2560 : 2560, 2003.

6. Defronozo R, Ferranine E. Insulin resistance : a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia and atherosclerotic disease. Diabetic Care 1991; 14 : 173- 94.

7. Pyorala M, Miettnen H, Laasko M. Insulin resistance syndrome predicts the risk of coronary heart disease and stroke in healthy middle aged men : the 22 year follow up results of the Insulin Policeman Study. Arteriscleros Thromb Vasc Biol 200; 20 538 – 44.

8. Christopher D. Byrne and Sarah H. Wild – The Metabolic syndrome – 1st ed pg 3.

9. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-52025 : prevalence, numerical estimates and projections. Diabetic Care 1988, 21 : 1415-31.

10. Sicree R, Shane J. Zimmet P. Diabetes and impaired glucose lolerance : In. Gran D. Diabetes Atlas International Diabetes Federation. 3rded Belgium : International Diabetic Federation; 2006 P-15-103.

11. Ahuja MMS. Epidemiological studies on diabetes mellitus in India. Epidemiology of diabetes in developing countries : 1979 P : 29-38.

12. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, et al. Diabetes epidemiology study group in India. (DESI). High prevalence of diabetes and impaired gluose tolerance in India. NUDS. Diabetologia 2001 : 44 : 1094 – 101.

13. Deepa M, Pradeepa R, Rama M, Mohan, et al. The Chennai Urban Rural Epidemiology study – the study design and epidemiology. JAPI 2003 ; 51 : 863 – 70.

14. Sowers JR, Epstein M, Frolich ED – Diabetes, Hypertension and cerebrovascular disease : an update. Hypertension 2001; 37 : 1053 – 1059.

15. Ferrannici E, Buzzigoli G, Bonadonna R et al. Insulin resistance in essential hypertension. NEJM 1987, 317 : 350 – 357.

16. Sten DC, Shieh SM, Fuh MM et al. Resistance to insulin stimulated glucose uptake in patients with hypertension. J Clin Endocrinol Metab 1988; 66 : 580 - 583.

17. Verdecchia P, Porcellati C, Schitillaci G, et al. Ambulatory blood pressure – An independent predictor of prognosis in essential hypertension. Hypertension 1994 : 24 : 793 – 801.

18. Nakano S, Kitazawa M, Tsuda et al. Insulin resistance is associated with reduced nocturnal fall of BP in normotensive, non obese type – 2 diabetic subjects. Clin Exp Hypertens 2002 ; 24 : 65 – 73.

19. White WB – A chronotherapeutic approach to the management of hypertension. Am J Hypertense 1996; 9 : 295 – 335.

20. Mogensen CE. Microalbuminuria and Hypertension with focus on type – 1 and type – 2 diabetes. J Intern Med 2003; 254 : 45 – 66.

21. Strecten DH. Pathogenesis of hyperadrenergic orthostatic hypertension - Evidence of disordered venous innervation exclusively in lower limbs. J Clin Invest ; 1990 : 86 : 1582 – 88.

22. Brett SE, Gopaul NK et al. Oral treatment with anti oxidant reduces oxidative stress and improves endothelial function in with type – 2 diabetes; Diabetologia 200; 4 : 974 – 77.

23. De Fronzo RA, Goldberg M, Agus ZS. The effects of glucose and insulin on renal electrolyte transport. J Clin Invest 1976; 58 : 83 – 90.

24. Wang CC, Coalstone ML, Draznin B. Molecular mechanisms of insulin resistance than impair cardiovascular biology. Diabetes 2004; 53 : 2735 – 2740.

25. Natali A, Santora D et al. Relationship between insulin release, antinatriuresis and hypokalemia after glucose ingestion in normal and hypertensive man. Clin Sci 1993; 85 : 327 – 35.

26. Hall JE, Summers RL, Resistance to metabolic actions of insulin and its role in hypertension. AM J Hypertens 1994; 7 : 772 – 88.

27. Morris AD, Connell JMC. Insulin and hypertension. J Hypertens 1994; 12 : 633 – 42.

28. Capron J, Jarnet J, Houset E, Growth promoting effects of diabetes and insulin on arteries; an in vivo study of rat aorta. Diabetes 1986 ; 35 : 973 – 8.

29. Hypertension in Diabetes Study Group. Increased risk of cardiovascular complications in hypertensive type – 2 diabetic patients. J Hypertens 1993 ; 11 : 319 – 25.

30. Lin JE, Roman NJ et al. The impact of diabetes in left ventricular filling pattern in hypertensive adults. J Am Coll Cardio 2001; 37 : 1949 – 9.

31. United Kingdom Prospective Diabetes Study Group. Tight BP control and risk of micro and macrovascular complications in type – 2 DM. UKPDS 38. BMJ 1998; 317 : 703 – 713.

32. Macmohan SW, Macdonald GJ, Antihypertensive treatment and plasma lipoprotein levels – The associations in data from a population study. Am J Med 1987; 80 : 40 – 47.

33. Kuperstein R, Hantly P – The importance of age and obesity on the relation between diabetes and left ventricular mass. J Am Coll Cardiol 2001; 37 : 1957 – 62.

34. Schernthaner G, Phillipp T, Ritz E. The significance of 24 hour BP monitoring in patients with DM. Dtsh Med Wochen schrift 1999; 124 : 393 – 5.

35. 1999 WHO – International Society of Hypertension Guidelines for the Management of Hypertension – guidelines subcommittee. J Hypertens 1999; 17 : 15 – 83.

36. Stamler J, Vaccaro O, Neaton JD – Diabetes and other risk factors and 12 year cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993; 16 : 434 – 44.

37. Pahor M, Psaty BM, Alderman et al. Health outcomes associated with calcium antagonists compared with other first line antihypertensive therapies : a meta analysis of randomized controlled trials. Lancet 2000; 356 : 1949 – 54.

38. Lithell HO. Effects of antihypertensive drugs on insulin, glucose and lipid metabolism. Diabetes Care 1991; 14 : 203 – 29.

39. Herings RM, Stricker BH, Porsius A – Hypoglycemia associated with use of inhibitor of ACE. Lancet 1995; 345 : 1195 – 98.

40. Lewis EJ, Hunsickler LG, Bain RP et al. The effect of ACE inhibition on diabetic nephropathy. NEJM 1993, 329 : 1456 – 62.

41. Effects of Ramipril on cardiovascular outcomes in people with DM : results of the HOPE study and MICRO – HOPE study. Lancet 2000; 355 : 253 – 9.

42. Ruilope L. RAS blockade : new possibilities in treatment of complications of diabetes. Heart 2000, 84 : 32 – 4.

43. Lindholm LH, Ibsen H, Dahlof et al. Cardiovascular mortality in patients with diabetes in Losartan Intervention for Endpoint reduction in hypertension study (LIFE) : a randomized control study against atenolol. Lancet 2002; 359 : 1004 – 8.

44. Lin JE, Roman NJ et al. The impact of diabetes in Left ventricular pattern of normotensive and hypertensive adults : the strong heart study. J Am Coll Cardiol 2001; 37 : 1943 – 9.

45. Flack JM, Hamaty M – Difficult to treat hypertensive populations – focus on African – Americans and people with Type 2 DM J. Hypertens 1999; 17 : 519 – 524.

46. Fischbacher C, Hunt S, Alexander – How physically active are South Asians in UK ? A literature review. J Public Health 2004. 26 250 – 58.

47. Ward AM, Fall C, Kumaran K, Veena S, Wood P et al Cortisol and metabolic syndrome in South Asians. Clin. Endocrinol 2003 ; 58 : 500 – 505

48. Bakris GL, Willians M et al, National. Kidney Foundation and Hypertension and Diabetes Executive Committee Working Group – Presenting renal function in adults with Hypertension and Diabetes : a consensus approach. Am J Kidney Dis, 36; 646 – 661.

49. Vasan RS, Larson MG, Leip et al. Impact of High Normal BP on the risk of Cardiovascular disease. Framingham Heart Disease NEJM 2001; 345 : 1291 – 97.

50. Sower JR, Frolich ED. Diabetes, Hypertension and Cardiovascular Disease – an update : Hypertens 2001 ; 37 : 1053 – 59.

ABBREVIATIONS

- ACE - Angiotensin Converting Enzyme.
- ADA - American Diabetic Association
- ATP- Adult Treatment Panel
- BMI - Body Mass Index
- BP - Blood Pressure
- CAD - Coronary Artery Disease
- CRP - C- Reactive Protein
- CURES - Chennai Urban Rural Epidemiological Study
- CVA - Cerebrovascular Accident
- DM - Diabetes Mellitus
- DR. Diabetic Retinopathy
- HDL.C- High Density Lipoprotein - Cholesterol
- HOT - Hypertension Optimal Treatment
- HT - Hypertension
- ICMR - Indian Council of Medical Research
- IFG - Impaired Fasting Glucose
- IGT - Impaired Glucose Tolerance
- ISH - Isolated Systolic Hypertension

- LDL - Low Density Lipoprotein
- NUDS - National Urban Diabetic Survey
- PDGF - Platelet Derived Growth Factor.
- PVD - Peripheral Vascular Disease
- TGL - Triglyceride
- UKPDS - United Kingdom Prospective Diabetes Study
- WHR - Waist/Hip Ratio
- WHO - World Health Organisation